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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,618	08/01/2003	David Lauffer	VPI/98-18 DIV US	4756

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EXAMINER	
HUANG, EVELYN MEI	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,618	LAUFFER ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) 4,9-11 and 14-21 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-3,5-8,12 and 13 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-21 are pending.

Election/Restrictions

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 3 and claims 1, 2, 5-8, 12, 13 in part , drawn to a compound of formula I or II wherein y=1, its composition and method of use thereof.

Group II, claim(s) 4, and claims 1, 2, 5-8, 12, 13 in part, drawn to a compound of formula I or II wherein Y=2, its composition and method of use thereof.

Group III, claim(s) 9-11, and 14-21, drawn to a composition comprising multiple active I ngredients, and its method of use.

3. The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the azabicyclo-[2.2.2]-octane of Group I and the azabicyclo-[2.2.1]-heptane of the Group II invention would not have been of sufficient similarity to allow for a Markush grouping to exhibit utility, absent some teaching of equivalence in the prior art. The composition of multiple active ingredients and the method of using multiple active ingredients of Group III is preoperly separate from the permissible combination of the product of Group I or II, a process especially adapted for the manufacture of the product, its composition and a use thereof.

4. During a telephone conversation with Mr. Govindaswamy on 2-27-2004 a provisional election was made with traverse to prosecute the invention of Group I, claim 3, and claims 1, 2, 5-8, 12, 13 in part. Affirmation of this election must be made by applicant in replying to this Office action. Claims of Group II and III are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

6. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-8, 12, 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1,

- It is unclear whether a compound or a mixture of the compound and pharmaceutically acceptable derivatives is being claimed. Rewriting the claim in the singular/alternative format is recommended, e.g. 'A compound....or a pharmaceutically acceptable salt thereof'.
- The term 'derivatives' in 'pharmaceutically acceptable derivatives' is open-ended and is therefore indefinite. It is recommended that its definition be positively recited in the claim.
- The term 'comprises' in 'each ring comprises' is open-ended and is therefore indefinite. Replacing it with 'is of' is recommended.
- Where on the bicyclic rings of formula I and II does the fusion with the benzene occur ? Fusion with just one benzene ring or 2 or more?

b. Claim 13, the amount of the compound administered to the patient or nerve cell is missing but is required in the method claim.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 3, 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Orlek (Re. 35593). The compound D21 (column 19, Description 21) is encompassed by the instant claims.

10. Claims 1, 3, 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Bulacinski AB (Acta Poloniae Pharmaceutica 1989, 46(5-6): 429-34). The compounds with RN 130877-60-0, 130877-61-1, 130877-65-5, 130877-62-2, 130877-63-3, 130877-64-4, 130877-66-6, are encompassed by the instant claims.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galliani (5015655).

Galliani generically discloses an azabicyclo compound (column 2, compound II) similar to the instant. Galliani's compound II wherein n=1, R1 = alkyl, alkenyl or alkynyl or alkyl substituted by arylalkyl is encompassed by the instant claims. An example wherein n=1 is shown on column 6, Example 15 and on column 7, Example 16. One of ordinary skill in the art would be motivated to prepare a compound II wherein n=1, R1 = alkyl, alkenyl or alkynyl or alkyl substituted by arylalkyl to arrive at the instant invention since Galliani has expressly taught such a compound within the small disclosed genus.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-8, 12, 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. ***.

Claims 1-41, 47-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is enabling only for the use of the compounds of claims 42-46 for neuroprotection against a chemotherapeutic agent such as taxol.

a. *Nature of the invention.*

The instant invention is drawn to an azabicyclo compound for stimulating neuronal regeneration in a patient suffering from a disease as recited in claim 17 or in an ex vivo nerve cell.

b. *State of the prior art and the level of the skill in the art.*

Compounds for promoting neuron differentiation in vitro are described by Novak (6268384). However, at present, there is no satisfactory treatment for neurological diseases associated with the death of or injury to neuronal cells (Novak, column 1, lines 20-30). The correlation between these in vitro assays and the in vivo effectiveness has not been established.

The level of the skill in the neuronal regeneration art is high.

c. *Predictability/unpredictability of the art.*

The high degree of unpredictability is well-recognized in the pharmaceutical art. A slight modification of the compound would drastically change its biological activity, as evidenced in the very different neurite outgrowth activities exhibited by the structurally similar compounds (Novak, column 43, Table 6). Furthermore, the in vitro activity is not always indicative of in vivo activity, as the nexus between these assays and the treatment of the diseases has not been established. For CNS drugs, whether the compound would cross the blood brain barrier would be of utmost importance, however, it cannot be predicted just from the structure of the compound.

d. *Amount of guidance/working examples.*

How to make

The general scheme for the preparation of the compounds is described. A specific example for the preparation of a species compound is not found in the specification. Indeed, not even a single example compound has been disclosed. Starting materials, such as HXCHAB and benzofused or multi-substituted azabicyclic [2.2.1] heptane carboxylic acid, the conditions and process of making these structurally diverse compounds as claimed are not seen but required. Sources are particularly pertinent, especially when the structures of the compounds are not fully

described. Absent sources, the public is offered mere language, rather than enablement. Ex parte Moersch 104 USPQ 122. In re Howarthe 210 USPQ 689.

How to use

The references for the assay procedures for assessing the neurotrophic effect are described. No results are shown. The nexus between the in vitro assay and the recited diseases has not been described in the specification.

e. *The breadth of the claims.*

Applicant's assertion that all the inventive compounds of diverse chemical structures (including those benzofused or multiple substituted azabicyclic [2.2.1] heptane, and those wherein the aryl, heteroaryl or heterocyclyl further substituted with multiple susbstituents) would be effective in stimulating neuronal regeneration in a patient having any of the diverse diseases recited does not commensurate with the scope of the objective enablement, especially in view of the high degree of unpredictability in the art, the absence of any working examples, and the known fact that at the time of the invention, there is no satisfactory treatment for neurological diseases, such as Alzheimer's diseases etc (paragraphs b-d above).

f. *Amount of undue experimentation.*

Since insufficient teaching and guidance have been provided in the specification (paragraphs b-e above), one of ordinary skill in the art, even with high degree of skill, would not be able to make and use the inventive compounds as claimed without undue experimentation.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 571-272-0693. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Evelyn Huang
Primary Examiner
Art Unit 1625

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